EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	10961	g-csf or hg-csf	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/02 12:36
L2	58	sun.in. and 1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/02 12:37
L3	6145	IgG4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/02 12:37
L4	1548	1 and 3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/02 12:37
L5	24	1 same 3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/02 12:37

```
Welcome to DIALOG

Dialog level 05.15.00D
? b 411;set files biotech
    02jan07 12:59:52 User219511 Session D669.2
       $0.00   0.115 DialUnits File410
   $0.00  Estimated cost File410
   $0.02  TELNET
   $0.02  Estimated cost this search
   $0.47  Estimated total session cost   0.245 DialUnits
File 411:DIALINDEX(R)

DIALINDEX(R)
  (c) 2007 Dialog

*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***
  You have 26 files in your file list.
  (To see banners, use SHOW FILES command)
? s (G-CSF or hG-CSF) and (IgG1 or IgG4)

Your SELECT statement is:
  s (G-CSF or hG-CSF) and (IgG1 or IgG4)

      Items   File
      -----   ----
          4   34: SciSearch(R) Cited Ref Sci_1990-2006/Dec W4
          2   71: ELSEVIER BIOBASE_1994-2007/Dec W5
          1   94: JICST-EPlus_1985-2006/Sep W2

  3 files have one or more items; file list includes 26 files.

? b 411;set files allscience
    02jan07 13:00:30 User219511 Session D669.3
       $1.21   0.410 DialUnits File411
   $1.21  Estimated cost File411
   $0.26  TELNET
   $1.47  Estimated cost this search
   $1.94  Estimated total session cost   0.655 DialUnits
File 411:DIALINDEX(R)

DIALINDEX(R)
  (c) 2007 Dialog

*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***
  You have 297 files in your file list.
  (To see banners, use SHOW FILES command)
? s (G-CSF or hG-CSF) and (IgG1 or IgG4)

Your SELECT statement is:
  s (G-CSF or hG-CSF) and (IgG1 or IgG4)

      Items   File
      -----   ----
          4   34: SciSearch(R) Cited Ref Sci_1990-2006/Dec W4
          2   71: ELSEVIER BIOBASE_1994-2007/Dec W5
    Examined  50 files
          1   94: JICST-EPlus_1985-2006/Sep W2
    Examined 100 files
    Examined 150 files
          3   440: Current Contents Search(R)_1990-2007/Jan 01
    Examined 200 files
    Examined 250 files

  4 files have one or more items; file list includes 297 files.

? s (G-CSF or hG-CSF) and (IgG1 or IgG4 or G1 or G4)

Your SELECT statement is:
  s (G-CSF or hG-CSF) and (IgG1 or IgG4 or G1 or G4)

      Items   File
      -----   ----
         10   5: Biosis Previews(R)_1969-2006/Dec W4
         14   34: SciSearch(R) Cited Ref Sci_1990-2006/Dec W4
          5   71: ELSEVIER BIOBASE_1994-2007/Dec W5
    Examined  50 files
          4   94: JICST-EPlus_1985-2006/Sep W2
    Examined 100 files
    Examined 150 files
         10   440: Current Contents Search(R)_1990-2007/Jan 01
    Examined 200 files
    Examined 250 files

  5 files have one or more items; file list includes 297 files.

? save temp; b 5,34,71,94,440;exs;rd
Temp SearchSave "TD355687210" stored
    02jan07 13:01:48 User219511 Session D669.4
       $7.62   2.591 DialUnits File411
   $7.62  Estimated cost File411
   $0.53  TELNET
   $8.15  Estimated cost this search
  $10.09  Estimated total session cost   3.245 DialUnits

SYSTEM:OS - DIALOG OneSearch
  File  5:Biosis Previews(R) 1969-2006/Dec W4
        (c) 2006 The Thomson Corporation
  File 34:SciSearch(R) Cited Ref Sci 1990-2006/Dec W4
        (c) 2006 The Thomson Corp
  File 71:ELSEVIER BIOBASE 1994-2007/Dec W5
        (c) 2007 Elsevier B.V.
  File 94:JICST-EPlus 1985-2006/Sep W2
        (c)2006 Japan Science and Tech Corp(JST)
  File 440:Current Contents Search(R) 1990-2007/Jan 01
        (c) 2007 The Thomson Corp

     Set  Items  Description
     ---  -----  ----------
Executing TD355687210
HILIGHT set on as '%'
        12855  G-CSF
           27  HG-CSF
        30001  IGG1
         7629  IGG4
        71202  G1
         8467  G4
     S1    43  (G-CSF OR HG-CSF) AND (IGG1 OR IGG4 OR G1 OR G4)
     S2    28  RD  (unique items)
? t s2/7/1-28;bye

 2/7/1    (Item 1 from file: 5)
DIALOG(R)File  5:Biosis Previews(R)
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0015787748  BIOSIS NO.: 200600133143
Phase II clinical study of rituximab and high-dose biweekly THP-COP
  (pirarubicin, cyclophosphamide, vincristine and predonisolone) with G-CSF
  for non-Hodgkin lymphoma: Results of a multicentric study of NMLSG
  (Niigata Malignant Lymphoma Study Group).
AUTHOR: Takizawa Jun (Reprint); Aoki Sadao; Takai Kazue; Kurasaki Tohri;
  Honma Keiichiro; Higashimura Masataka; Nagai Kourichi; Momoi Akihito;
  Nikkuni Koji; Aizawa Yoshufusa
AUTHOR ADDRESS: Niigata Univ, Med and Dent Hosp, Div Hematol, Niigata,
  Japan**Japan
JOURNAL: Blood  106 (11, Part 2): p264B NOV 16 2005 2005
CONFERENCE/MEETING: 47th Annual Meeting of the
American-Society-of-Hematology  Atlanta, GA, USA  December 10 -13, 2005;
20051210
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SPONSOR: Amer Soc Hematol
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Introduction CHOP chemotherapy has been accepted as the standard treatment for patients with non-Hodgkin lymphoma (NHL), but in some histological or clinical subtypes the results are not satisfactory. We have shown the efficacy and safety of high-dose biweekly THP-COP with G-CSF support (HDBW-TCOP(G)) for NHL. In this regimen, we choose pirarubicin in stead of doxorubicin because it was proven high efficacy against NHL and the lower toxicity than doxorubicin. Recently, the combination of rituximab and standard CHOP has been shown to have a synergistic effect for NHL. We performed a phase II multicentric clinical study to assessed the feasibility and toxicity of the combination chemotherapy of rituximab and HDBW-TCOP(G) (HDBW-R-TCOP(G)) compared with those of HDBW-TCOP(G).Patients and methods Between August 1998 and December 2004, Forty-one Japanese patients with previously untreated NHL from whom informed consent was obtained were included in this study. Median age was 45 (range 19-63) years. There were 19 males and 22 females.According to WHO-classification diagnoses, histological subtypes included follicular lymphoma (FL) 15(37%); nodal marginal zone B-cell lymphoma (NMZBCL) 2(5%); mantle cell lymphoma (MCL) 3(7%); anaplastic large cell lymphoma (ALCL) 1(2%), diffuse large B-cell lymphoma (DLBCL) 18(44%); peripheral T-cell lymphoma (PTCL) 1(2%), angioimmunoblastic T-cell lymphoma (AILT) 1(2%). Of 41 patients, one patient was stage 1, stage 2, 11 stage 3 and 16 stage 4. International prognostic index (IPI) included L 6; LI 22; HI 7; H 6. HDBW-TCOP(G) consisted of pirarubicin 70 mg/m(2) on day 1; cyclophosphamide 1000 mg/m(2) on day 1; vincristine 1.4 mg/m(2) on day 1; predonisolone 50 mg/m(2) orally from day 1 to 5; lenograstim 2.0 mu g/kg/day from day 3. Fifteen patients who enrolled after rituximab was approved in Japan received therapy combined HDBW-TCOP(G) with rituximab 375mg/m(2) on day -2 (HDBW-R-TCOP(G)). Six cycles were administered at intervals of two weeks.Results Of the 41 patients treated, 32 (78.0%) achieved a complete remission (CR) and nine (22.0%) achieved a partial remission (PR), for an overall response rate of 100%. After median follow-up of 36 months (range 2.9-81.8), progression free survival (PFS) and overall survival (OS) were 68.2% and 97.5%, respectively. PFS was 90.9% for HDBW-R-TCOP(G), and 69.5% for HDBW-TCOP(G), but no significant differences was found among two regimen. There was no significant difference in the PFS and OS between aggressive and indolent histological subtypes. 76% of patients developed Grade 4 leukopenia (according to NCI criteria) but no patients experienced febrile neutropenia. 15% of patients developed %G4% anemia and 17% of patients %G4% thrombocytopenia. Other adverse effects were minimal.Conclusion Both HDBW-TCOP(G) and HDBW-R-TCOP(G) are feasible for NHL with acceptable toxicity. The excellent result suggests they are effective for aggressive NHL patients with poor prognostic factors and advanced stage indolent NHL.

2/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0015132389 BIOSIS NO.: 200500039454
Long-survival in responding patients with metastatic breast cancer treated with doxorubicin-docetaxel combination. A multicentre phase II trial
AUTHOR: Mattioli R; Lippe P (Reprint); Massacesi C; Cappelletti C; Nacciarriti D; Bisonni R; Graziano F; Menichetti E T; Imperatori L; Testa E; Laici G; Balletta A; Silva R R
AUTHOR ADDRESS: Med Oncol Unit, S Croce Hosp, I-61032, Fano, Italy**Italy
AUTHOR E-MAIL ADDRESS: paolippe@libero.it
JOURNAL: Anticancer Research 24 (5B): p3257-3261 September 2004 2004
MEDIUM: print
ISSN: 0250-7005
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: The doxorubicin-docetaxel combination is active in breast cancer; the aim of the present study was to evaluate the complete response rate and safety profile of the doxorubicin and docetaxel regimen as first-line chemotherapy in metastatic breast cancer patients. Patients and Methods: Forty-three patients entered the study. Treatment plan was: doxorubicin (50 mg/m2 i.v. bolus) followed 1 hour later by docetaxel (75 mg/m2, i.v. infusion over 1 hour), q 3 weeks, for up to six courses. The patients achieving a response or a stabilisation of disease after 6 courses were allowed to intensify the treatment with docetaxel (100 mg/m2, q 3 weeks) for up to 2 courses. G-CSF (or GM-CSF) was administered if clinically indicated. Results: Patients' median age was 57 years (range 32-75) and 72% of them had visceral disease. A total of 217 doxorubicin-docetaxel courses were delivered, with 70% of patients receiving all the 6 planned cycles. Among the 40 patients assessable for response (WHO criteria), 7 (16%) achieved a complete remission and 22 (51%) a partial remission, for an overall response rate (intent-to-treat) of 67% (95% C.I. = 53% to 81%). In 19 patients, the treatment was intensified with two more single-agent docetaxel cycles, without ameliorating the response. Twenty-seven patients with oestrogen receptor-positive received hormonal therapy as 'maintenance' after completing chemotherapy treatment. NCIC G3-%G4% neutropenia was recorded in 58% of patients, with G/GM-CSF used in 23 (53%) patients and 91 (38%) cycles. No patients experienced severe cardiac or neurological toxicity. No toxic death occurred. With a median follow-up of 41 months among alive patients, we observed in responder patients an overall median time to progression and survival of 18 and 33 months respectively, with ten long-survivors still alive. Conclusion: This study confirmed the combination doxorubicin-docetaxel as a very active regimen for metastatic breast cancer. Remarkably long survival times were observed not only in complete responders, but also in those patients who responded partially. This might be equally attributed to first-line treatment and sequential maintenance hormonal therapy.

2/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014814184 BIOSIS NO.: 200400181870
Selective isolation of a low proliferative pluripotent progenitor cell from umbilical cord blood mononuclear cells using the complimentary effect of Methotrexate and Leucovorin.
AUTHOR: Akabutu John J (Reprint); Chan John
AUTHOR ADDRESS: Alberta Cord Blood Bank, Edmonton, AB, Canada**Canada
JOURNAL: Blood 102 (11): p424b-425b November 16, 2003 2003
MEDIUM: print
CONFERENCE/MEETING: 45th Annual Meeting of the American Society of Hematology San Diego, CA, USA December 06-09, 2003; 20031206
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The ideal input progenitor cell capable of self renewal, expansion, differentiation and cellular transduction remains unknown. This putative progenitor is believed to be quiescent and to reside in the G0/%G1% interphase of the cell cycle. Therefore, 'S' phase specific antimetabolites, such as Methotrexate (MTX) should have little effect on the survival of these cells. They may however prevent the entry of these cells into the cell cycle through the inhibition of DNA and protein synthesis. Transport and inhibition by MTX is optimized for sensitive cells that are actively synthesiszing DNA and protein in the 'S' phase of the cell cycle. Leucovorin (LV) can block this inhibition and thus prevent cellular apoptosis. This maneuver has been clinically effective in the prevention of excessive bone marrow toxicity following high to moderate dose MTX therapy for some malignant diseases especially in children. The complimentary effect of MTX/LV was used as a tool to select for a low proliferative progenitor cell from fresh human umbilical cord

blood. Ficol-Hypaque density gradient fractionated mononuclear cells (MNCs) from fresh human umbilical cord blood were exposed to MTX for a 4 day period in a liquid culture system. On day 5, LV was added to the culture and the incubation was continued. The cells were harvested on day 8 and were re-fractionated on a Ficol-Hypaque density gradient. They were then cultured in a methylcellulose assay for CFU with the cytokines G-CSF, GM-CSF and Epo. 15% of the MNCs remained viable after treatment with MTX/LV. <1% of the surviving cells stained positively for the CD34 surface marker. The CFU rate of colony formation was 2.4 per 105 cells for the treated cells compared with 380 per 105 cells plated for the controls. All hematopoietic lineages were present in the MTX/LV treated colonies. We conclude that, MTX/LV selects for a low proliferative cohort of mostly CD34 negative cells that may represent more primitive progenitor cells present in human umbilical cord blood. They are capable of being induced to form colonies of myeloid/erythroid cells when exposed to hematopoietic cytokines. These low proliferative progenitors may prove to be ideal input cells for ex-vivo expansion programs and for cellular transduction experiments. Further investigations of the effect(s) of non-hematopoietic growth factors/cytokines on these unique progenitor cells from human umbilical cord blood are warranted.

2/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014781832 BIOSIS NO.: 200400148493
Alternatively spliced c-myb mRNA transcripts play a role in hematopoietic cell development, and can reverse Bcr/Abl induced maturation arrest in 32D cells.
AUTHOR: Zou Shaomin (Reprint); Swider Cezary R; Hsu June (Reprint); Kalota Anna (Reprint); Millholland John M (Reprint); Gewirtz Alan M (Reprint)
AUTHOR ADDRESS: Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA, USA**USA
JOURNAL: Blood 102 (11): p852a-853a November 16, 2003 2003
MEDIUM: print
CONFERENCE/MEETING: 45th Annual Meeting of the American Society of Hematology San Diego, CA, USA December 06-09, 2003; 20031206
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Poster; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The c-myb protooncogene encodes a transcription factor (c-Myb) which is required for normal, and malignant, hematopoietic cell development c-Myb likely plays a role in leukemogenesis but the mechanisms involved are not completely defined. To this end, we have searched for potential c-Myb activating mutations, deletions, and splice variants in leukemia cells, and have found two splice variants, one novel, and one previously known, that might prove informative. The novel variant was identified in K562 cells and found to lack the entire 3rd exon of wild type c-myb (myb-wt). This exon encodes 24 amino acids of the DNA binding domain. The variant mRNA species was present in amounts equal to myb-wt mRNA, and interestingly, was not found in normal lymphocyte total cellular RNA (n=6). The known splice variant, (myb-9), lacks nine base pairs in the transactivation domain which results in an in-frame loss of three amino acids, Val-Leu-Pro. Myb-9 has been found in both normal and leukemic blood cells, but of significant interest, the ratio of myb-9 to myb-wt, varies directly with cell maturation. In leukemic patient blood samples (n=22), the myb-9/myb-wt mRNA expression ratio, as measured by quantitative real-time PCR (QRT-PCR), ranged from 0.0 (n=11) to 0.7. Myb-9 expression was not related to cell cycle position when measured in K562 cells FACS sorted into G0/%G1%, S, and G2/M populations. Based on these, and other results, we hypothesized that myb-9 promoted cellular maturation. This theory was further tested by investigating the effect of myb-wt and myb-9 overexpression on the ability of Bcr/Abl expressing 32D cells (32D.p210- kind gift of B. Calabretta, Thomas Jefferson University) to undergo maturation. The 32D or 32D.p210 cells were transduced with a pHMD lentiviral vector in which full length myb-9 (pHMD.Myb-9), or myb-wt (pHMD.myb-wt), cDNA was sub-cloned upstream of an internal ribozyme entry site (IRES)-GFP reporter cassette. FACS analysis on GFP+ cells for the granulocyte marker Mac-1 was then conducted. Mac-1 was constitutively expressed on 97.6% of parental 32D cells, but was undetectable on 32D.p210 cells. Transduction of 32D.p210 cells with pHMD expressing only GFP, or pHMD.myb-wt, failed to induce Mac-1 expression, even in the presence of G-CSF. In marked contrast, in 32D.p210 cells transduced with pHMD.myb-9, Mac-1 expression was restored to parental 32D cell levels, even in the absence of G-CSF stimulation. Similar results were obtained with another granulocyte marker, Gr-1. When G-CSF stimulated, Gr-1 was detected on 92% parental of 32D cells, but on not on 32D.p210. Such cells remained Gr-1 (-), even in the presence of G-CSF, when transduced with various control pHMD vectors, and with pHMC.myb-wt. In marked contrast, infection of 32D.p210 with pHMD.myb-9 reversed the block in G-CSF response leading to parental cell expression levels of Gr-1 in GFP+ cells only. The mechanism of rescue remains under investigation. It is not a simple competition since both forms of c-Myb are fully functional in Luciferase reporter assays carried out in 293T cells, and one does not compete in such assays for the other. In conclusion, we have identified at least one, and possibly two, myb splice variants that appear to play an important role in regulating hematopoietic cell differentiation. The molecular mechanisms which allow these variants to help regulate hematopoietic cell maturation should give important new insights into c-myb's role in normal and leukemic hematopoietic cell development.

2/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014780906 BIOSIS NO.: 200400147567
Myeloid growth factors are requied for the differentiation of acute promyelocytic leukemia (APL).
AUTHOR: Matsui William (Reprint); Smith B D (Reprint); Vala Milada (Reprint); Beal Nikeshia (Reprint); Jones Richard J (Reprint)
AUTHOR ADDRESS: Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA**USA
JOURNAL: Blood 102 (11): p608a-609a November 16, 2003 2003
MEDIUM: print
CONFERENCE/MEETING: 45th Annual Meeting of the American Society of Hematology San Diego, CA, USA December 06-09, 2003; 20031206
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Differentiation therapy with all-trans-retinoic acid (ATRA) has dramatically improved outcomes in patients with APL. It is known that myeloid growth factors (e.g., G-CSF and GM-CSF) enhance the differentiation of APL cells when combined with ATRA, and we recently reported that growth factors are required for the maximal activity of various pharmacologic differentiating agents in non-APL acute myeloid leukemia (Matsui et al., Cell Growth Diff., 2002). Therefore, we studied the role of growth factors in the differentiation of APL. We found that G-CSF (200 U/ml) or GM-CSF (200 U/ml) augmented ATRA (10-6 M)-induced differentiation of the human APL cell line NB4, as evidenced by increased expression of the myeloid antigens CD15 and CD11b and further inhibition of clonogenic growth. Similarly, both growth factors enhanced the differentiation of leukemic blasts obtained from clinical specimens of 6 patients with newly diagnosed APL when combined with ATRA. Moreover, growth factors were required for ATRA's activity as neutralizing monoclonal antibodies against G-CSF, GM-CSF, and IL-3 blocked the effects of ATRA on both NB4 and clinical APL cells. Our previous data also demonstrated that growth factors primarily induce tumor cell differentiation, rather than proliferation, when combined with agents that block cell cycling; therefore, we further studied the effects of growth factors on the activity of two unrelated agents, arsenic trioxide (As2O3) and bryostatin-1 (bryo) in APL. As with ATRA, As2O3 (10-6 M) and

bryo (10-8 M) inhibited cell cycling of NB4 cells at %G1% without causing apoptosis. Furthermore, each agent induced a modest degree of differentiation of both NB4 and clinical APL cells that could be enhanced by G-CSF and inhibited by anti-growth factor neutralizing antibodies. Pharmacologic differentiating agents, including ATRA, do not appear to be sufficient for inducing the maturation of APL cells. Rather, these data suggest that myeloid growth factors may serve as the primary differentiating agents in APL since they are required for the activities of ATRA, As2O3 and bryo. The ability of ATRA and other pharmacologic differentiating agents to inhibit cell cycling may selectively enhance the differentiating activity of growth factors by blocking their proliferative effects. Furthermore, the maximal induction of terminal differentiation requires both cell cycle inhibitors and growth factors.

2/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014780823 BIOSIS NO.: 200400147484
C/EBPalphap30, a myeloid leukemia oncoprotein, limits G-CSF Receptor expression but not terminal granulopoiesis via site-selective inhibition of C/EBP DNA-binding.
AUTHOR: Friedman Alan D (Reprint); Cleaves Rebecca (Reprint); Wang Qian-Fei (Reprint)
AUTHOR ADDRESS: Pediatric Oncology, Johns Hopkins University, Baltimore, MD, USA**USA
JOURNAL: Blood 102 (11): p587a November 16, 2003 2003
MEDIUM: print
CONFERENCE/MEETING: 45th Annual Meeting of the American Society of Hematology San Diego, CA, USA December 06-09, 2003; 20031206
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Poster; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Heterozygous mutations of the CEBPA gene are present in 5% of acute myeloid leukemia (AML) cases and often lead to the expression of an N-terminally truncated, 30 kilodalton isoform, C/EBPalphap30, from an internal translation start site. We have assessed the affect of C/EBPalphap30 on granulopoiesis utilizing C/EBPalphap30-ER, containing the estradiol receptor ligand-binding domain. In contrast to C/EBPalpha-ER, C/EBPalphap30-ER did not induce 32Dcl3 myeloid cell differentiation in IL-3. However, both isoforms were capable of inhibiting E2F activity in 32Dcl3 cells and of slowing their %G1% to S progression. Inhibition of E2F in this lineage by C/EBPalphap30, but not in NIH 3T3 cells, might reflect interaction of C/EBPalpha with different co-repressor molecules in different lineages. C/EBPalphap30 reduced expression of the endogenous G-CSF Receptor (GCSFR) several-fold, as assessed by FACS analysis of surface GCSFR expression and by Northern blotting. To facilitate investigation of the effect of C/EBPalphap30-ER on granulopoiesis downstream of G-CSF signalling, we co-expressed exogenous G-CSFR. C/EBPalphap30-ER/GCSFR cells expressed several granulocytic markers in G-CSF, including MPO, lysozyme, C/EBPepsilon, and PU.1 and demonstrated nuclear maturation. As we observed selective inhibition of GCSFR expression by C/EBPalphap30, we considered the possibility that this might be due to reduced affinity of C/EBPalphap30 for the C/EBP site in the GCSFR promoter compared to other C/EBPalpha target genes. Rat C/EBPalpha-ER and C/EBPalphap30-ER, expressed in 293T cells, bound the C/EBP site from the NE gene with similar affinity, as did human C/EBPalpha and C/EBPalphap30. In contrast, C/EBPalphap30 bound the C/EBP sites in the GCSFR gene with 7-fold reduced affinity and bound the C/EBPalpha site in the PU.1 gene with 3-fold reduced affinity. Thus, the selective inhibition of GCSFR expression by C/EBPalphap30-ER is due in part to its variable affinity for C/EBP sites. Acute myeloid leukemias harboring C/EBPalphap30 might therefore by blocked in their maturation due to lack of GCSFR and in addition may harbor additional mutations, for example in the cdk/cyclin/Rb pathway, which overcome cell cycle inhibition mediated by C/EBPalphap30. Variation in affinity for selected cis elements amongst protein isoforms, arising due to internal translation initiation or alternative splicing, may affect the biology of basic region-leucine zipper (bZIP) proteins in general.

2/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014408986 BIOSIS NO.: 200300367705
Effects of 5-aza-2'-deoxycytidine (DAC, decitabine) on Proliferation and Differentiation of Cytokine-Expanded Normal Human CD34+ Cells: A Model for Methylation Changes during Myeloid Maturation.
AUTHOR: Guo Yalin (Reprint); Engelhardt Monika (Reprint); Wider Dagmar (Reprint); Claus Rainer (Reprint); Lubbert Michael (Reprint)
AUTHOR ADDRESS: Hematology/Oncology, University of Freiburg Medical Center, Freiburg, Germany**Germany
JOURNAL: Blood 100 (11): pAbstract No. 4221 November 16, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 44th Annual Meeting of the American Society of Hematology Philadelphia, PA, USA December 06-10, 2002; 20021206
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Poster; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: DNA methylation is a major epigenetic mechanism controlling tissue- and development-specific gene regulation. During normal hematopoietic cell maturation, methylation of myeloid-specific genes (e.g. myeloperoxidase (MPO), lysozyme (LZM), CSF receptors) is decreased concomitantly with differentiation (Blood 87:447-455,1996; Leukemia 13:530-534, 1999). Conversely, the S-phase-specific demethylating agents 5-azacytidine and 5-aza-2'-deoxycytidine (DAC) have shown a moderate differentiation-inducing activity on myeloid cell lines. To establish an in vitro model of normal hematopoietic differentiation modulated by demethylation, we used CD34+ cells from apheresis specimens (AP) and analyzed proliferation, viability, CD15, LZM and MPO expression (FACS) with and without DAC treatment. Since DAC is ineffective on cells in G0, CD34+ cells from AP (being mostly in G0/%G1%) were cultured with serum containing medium (IMDM plus 10% FCS) (SCM, n=4) or serum-free medium (SFM, n=10) in the presence of Flt3, SCF, and IL-3 for 72 hours. Treatment with DAC was performed on day (d) 3 of culture, as three 24hr pulses with two low-cytotoxic concentrations (10, 50 nM). Cells were harvested on d7 of culture. Without DAC treatment, cell expansion under these conditions was 11.9 fold (range 0.36 - 22.8). With DAC pretreatment, growth inhibition was observed relatively to the expansion culture (median 13.9%, range -4.4 - 27.6% (10 nM DAC); median 17.3%, range -13.9 - 47.7% (50 nM DAC)), as well as a slightly decreased cell viability (median 8.8%, range -5.8 - 46% (10 nM DAC); median 17.7%, range -23.3 - 73.1% (50 nM DAC)). Interestingly, DAC induced an increase in LZM+ cells (median 14.1%, range 4.3 - 36.8% (10 nM DAC); median 19.8%, range 8 - 56.5% (50 nM DAC), n=7), and a lesser increase in MPO+ cells (median 0.4%, range -10.2 - 17.5% (10 nM DAC); median 5.3%, range -9 - 19.5% (50 nM DAC)) and CD15+ cells (median 7.6%, range -10.8 - 22.4% (10 nM DAC); median 4.6%, range -24.7 - 33.8% (50 nM DAC)). In order to ask whether DAC pretreatment increases responsiveness of the cells to G-CSF, DAC treatment was followed by G-CSF (10 mg/ml) for 48 hours. Expectedly, G-CSF alone led to a substantial increase of LZM+ cells (median 36.7%, range 33 - 86.8%, n=5), MPO+ cells (median 21.1%, range 3.8 - 22.6%) and CD15+ cells (median 26.2%, range 14.8 - 44.1%). With DAC pretreatment, we detected an additive increase in LZM+ cells upon G-CSF-induced differentiation (median 49.1%, range 13 - 127.4% (10 nM DAC); median 50.8%, range 39.1 - 63.2% (50 nM DAC)), whereas no additional effect on expression of MPO (median 19.4%, range 4.6 - 50.5% (10 nM DAC); median 20.2%, range 6.8 - 29.8% (50 nM DAC)) or CD15 (median 23.7%, range -21.6 - 44% (10 nM DAC); median 33.2%, range 6.5 - 62.5% (50 nM DAC)) was noted. In conclusion, at low-cytotoxic concentrations DAC induces a dose-dependent inhibition of cell growth, and moderately increases differentiation markers in cytokine-expanded normal hematopoietic

precursor cells. This effect was particularly evident for lysozyme expression. This model should be suitable for global analyses of multiple differentially methylated genes, to determine possible patterns of methylation and gene expression being established during lineage-specific maturation.

2/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014398274 BIOSIS NO.: 200300356993
All-Trans Retinoic Acid (ATRA) Endows G-CSF Responsiveness to NB4 Cells Via Upregulation of the G-CSF Receptor.
AUTHOR: Enriquez Louie (Reprint); Maun Noel (Reprint); Khanna-Gupta Arati (Reprint); Zibello Theresa (Reprint); Gaines Peter (Reprint); Berliner Nancy (Reprint)
AUTHOR ADDRESS: Department of Internal Medicine, Yale University School of Medicine, New Haven, CT, USA**USA
JOURNAL: Blood 100 (11): pAbstract No. 2859 November 16, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 44th Annual Meeting of the American Society of Hematology Philadelphia, PA, USA December 06-10, 2002; 20021206
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Several lines of investigation suggest that G-CSF can augment all-trans retinoic acid (ATRA)-induced neutrophil differentiation in acute promyelocytic leukemia (APL). Using EPRO cells overexpressing the G-CSF receptor (EPRO-GR), we showed previously that ATRA and G-CSF appear to regulate neutrophil differentiation by divergent pathways (Blood Vol 98, Supp. 1, p290a,2001). ATRA-mediated differentiation of EPRO-GR cells occurs via a retinoic acid response element (RARE)-dependent, STAT-independent pathway, while G-CSF-mediated differentiation occurs via a RARE-independent, STAT-dependent pathway. Here we examined G-CSF-mediated and ATRA-mediated differentiation in the APL cell line, NB4. As reported by others, we observed that G-CSF in the absence of ATRA is incapable of inducing NB4 cell maturation. However, ATRA induction of NB4 cells results in marked upregulation of G-CSFR mRNA and protein. G-CSFR does not appear to be a direct target of ATRA, since transcriptional upregulation does not occur in the presence of cycloheximide. ATRA-mediated differentiation of NB4 cells is associated with upregulation of G-CSFR, but not phosphorylation of STAT3 (Tyr 705), a critical signaling event during G-CSFR-mediated differentiation. ATRA-induced NB4 cells subsequently exposed to G-CSF show STAT3 phosphorylation, suggesting that ATRA enables the acquisition of G-CSF responsiveness. We then further characterized the effects of G-CSF alone on NB4 cells rendered G-CSF responsive by 24 hour exposure to ATRA (ATRA'apprx>G-CSF). NB4 cells primed with ATRA and then placed into growth medium were used as a control (ATRA'apprx>Uninduced). Morphologic differentiation is seen in both ATRA'apprx>G-CSF and ATRA'apprx>Uninduced cells. Cell cycle analysis by flow cytometry for incorporation of propidium iodide (PI) showed that ATRA-mediated differentiation is associated with a marked decrease in the percentage of cells in the S-phase (15.05%) and the G2/M-phase (3.22%) when compared to uninduced cells (S-phase: 54.3%; G2/M-phase: 9.04%). This decreased proliferation is associated with morphologic maturation. In contrast, G-CSF exposure does not alter the cellular proliferation of NB4 cells (S-phase: 56%; G2/M-phase: 5.79%) when compared with uninduced cells. ATRA'apprx>G-CSF (G0/%G1%-phase: 69.69%) and ATRA'apprx>Uninduced (G0/%G1%-phase: 76.82%) cells both revealed cell cycle arrest. To assess the correlation of G-CSF surface expression with total mRNA and protein levels we used flow cytometry for biotinylated G-CSF binding. In this analysis, G-CSFR was upregulated in both ATRA'apprx>G-CSF and ATRA'apprx>Uninduced cells. Because ATRA-induced differentiation proceeds autonomously in NB4 cells after only a short exposure to ATRA, we were unable to distinguish an independent role for G-CSF in the induction of maturation in this model. However, the observation that the initial expose to ATRA makes NB4 cells capable of G-CSF-dependent STAT signaling leads us to hypothesize that ATRA-induced upregulation of G-CSFR may induce G-CSF responsiveness in primary APL cells. We speculate that it may explain the reported response of t(11;17) APL (which is ATRA-resistant) to the combination of ATRA and G-CSF. Further characterization of the molecular events underlying these distinct pathways may further elucidate the mechanism of G-CSF augmentation of ATRA effects and may lead to novel therapeutic approaches to APL.

2/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014378981 BIOSIS NO.: 200300335724
Ex-Vivo Expansion of SCID-Repopulating Cell Activity under Hypoxic Conditions.
AUTHOR: Danet Guenahel H (Reprint); Luongo Jennifer L (Reprint); Pan Yi (Reprint); Bonnet Dominique (Reprint); Simon M Celeste (Reprint)
AUTHOR ADDRESS: Abramson Family Cancer Research Institute, University of Pennsylvania, Philadelphia, PA, USA**USA
JOURNAL: Blood 100 (11): pAbstract No. 1124 November 16, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 44th Annual Meeting of the American Society of Hematology Philadelphia, PA, USA December 06-10, 2002; 20021206
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Poster; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: It has been shown that murine hematopoietic stem cells are more concentrated in the low oxygen areas of the bone marrow (BM). In addition, the repopulating activity of cultured mouse BM is preferentially enhanced under severe hypoxic conditions. The aim of this study was to characterize the functional and molecular effects of hypoxia on cultured human hematopoietic progenitors and stem cells. Lineage-negative (Lin-) CD34+ or CD34+CD38- cells were isolated from normal adult BM and cultured for 4 days in hypoxia (1% or 3% O2) or normoxia (18% O2) in serum-free medium in the presence of IL-3, IL-6, G-CSF, SCF and FLT-3 ligand. In hypoxic conditions, Lin-CD34+ cells and primitive CD34+ subsets (CD38-, CD90+, HLA-DR-, CXCR4+) divided at a slower rate (CFSE tracking) compared to normoxia, resulting in fewer cells after 4 days in culture. In contrast, Lin-CD34+ CD38- cells expanded faster in hypoxia than in normoxia. Hypoxic cultures were also associated wih a higher frequency of Lin-CD34+ cells in G0/%G1% phase (65.8+-3.1% vs 53.7+-4% in normoxia) and with a higher proportion of cells in %G1% phase based on Ki-67 expression. Functionally, there was no significant difference in the frequency of CFC or LTC-IC detected in hypoxic and normoxic cultures at Day 4. The bone marow-repopulating activity of Lin-CD34+CD38- cells was evaluated at Day 0, 4, 6 and 9 (1%, 3% and 18% O2) using the NOD/SCID mouse model. SCID-repopulating cell (SRC) activity in cultured cells was dectectable until Day 4 but was no longer present at Day 6 or 9, regardless of oxygen levels. Using limiting dilution analysis, we determined that, at Day 4, there was no significant difference in SRC activity between cells cultured in 3% O2 and 18% O2. However, SRC activity was increased in cells cultured at 1% O2 (1 SRC in 700 cells) compared to normoxia (1 SRC in 2,000 cells). After 4 days at 1% O2, SRC activity was even greater than in freshly isolated Lin-CD34+CD38- cells (1 SRC in 900 cells) indicating that human hematopoietic stem cells can be sustained and even expanded in vitro under severe hypoxic conditions. We also characterized the molecular response of human BM Lin-CD34+ CD38- cells to hypoxia. Using RT-PCR, we determined that freshly isolated cells express hypoxia-inducible factor 1alpha (HIF-1alpha) and arylhydrocarbon receptor nuclear translocator protein (ARNT) but not HIF-2alpha. Under severe hypoxia, HIF-1alpha protein levels increased, and cell surface expression of Flt-1(VEGF-R1), KDR (VEGF-R2), and Tie-2 was upregulated while HLA-DR and von Willebrand factor surface expression was down regulated. Interestingly, VEGF

secretion from Lin-CD34+ cells was 2.3 fold higher in hypoxic cultures, suggesting that VEGF could play an important role in the maintenance or expansion of human stem cell activity under severe hypoxia.

2/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0010740228 BIOSIS NO.: 199799374288
The unexpected G0/%G1% cell cycle status of mobilized hematopoietic stem cells from peripheral blood
AUTHOR: Uchida Nobuko (Reprint); He Dongping; Friera Annabelle M; Reitsma Michael; Sasaki Dennis; Chen Ben; Tsukamoto Ann
AUTHOR ADDRESS: Systemix Inc., 3155 Porter Dr., Palo Alto, CA 94304, USA** USA
JOURNAL: Blood 89 (2): p465-472 1997 1997
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Treatment with a combination of cytokines and chemotherapy can effectively stimulate the release of hematopoietic stem cells (HSC) into the peripheral blood (PS), which can then be harvested for transplantation. The cell cycle status of the harvested HSC from mobilized PB (MPB) is of interest because of the impact that cell cycling may have on optimizing the conditions for ex vivo expansion, retrovirus-mediated gene transfer, and the engraftment of transplanted tissues. Therefore, we characterized the cell cycling status of mobilized HSC from mice and humans. The murine HSC which express the phenotype c-kit+ Thy-1.1-lo Lin-/lo Sac-1+, were purified from PB, bone marrow (BM), and spleen after the mice were treated with the mobilizing regimen of granulocyte colony-stimulating factor (G-CSF) or a combination of cyclophosphamide (CTX) and G-CSF. Human HSC (CD34+ Thy-1+ Lin-) and progenitor cells (CD34+ Thy-1- Lin-) were isolated from the BM of untreated healthy volunteers and from MPB of healthy volunteers and patients treated with G-CSF or a combination of CTX and GM-CSF. Cell cycle status was determined by quantitating the amount of DNA in the purified cells after staining with the dye Hoechst 33342. Fluorescence-activated cell sorting analysis of the progenitor cells from the murine and human samples showed an unexpected finding, ie, virtually none of the cells from the MPB was cycling. The G0/%G1% status of HSC from MPB was surprising, because a significant proportion of HSC from BM are actively proliferating and, after mobilization, the HSC in the spleen and BM were also actively cycling.

2/7/11 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

14303855 Genuine Article#: 960EE Number of References: 13
Title: Cost effectiveness of day 5 G-CSF (Lenograstim (R)) administration after PBSC transplantation: results of a SFGM-TC randomised trial
Author(s): Valteau-Couanet D (REPRINT) ; Faucher C; Auperin A; Michon J; Milpied N; Boiron JM; Bourhis JH; Gisselbrecht C; Vernant JP; Pinna A; Bendahmane B; Delabarre F; Benhamou E
Corporate Source: Inst Gustave Roussy,Dept Paediat,39 Rue Camille Desmoulins/F-94800 Villejuif//France/ (REPRINT); Inst Gustave Roussy,Dept Paediat,F-94800 Villejuif//France/; Inst J Paoli I Calmettes,F-13009 Marseille//France/; Inst Gustave Roussy,Dept Stat,F-94800 Villejuif//France/; Inst Curie,Paris//France/; CHU Nantes,F-44035 Nantes//France/; CHU Bordeaux,Bordeaux//France/; Inst Gustave Roussy,Adult Med Dept,F-94800 Villejuif//France/; St Louis Hosp,Paris//France/; Grp Hosp Pitie Salpetriere,F-75634 Paris//France/; Labs Chugai & Aventis,Paris//France/(valteau@igr.fr)
Journal: BONE MARROW TRANSPLANTATION, 2005, V36, N6 (SEP), P547-552
ISSN: 0268-3369 Publication date: 20050900
Publisher: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
Language: English Document Type: ARTICLE
Abstract: This randomised trial was designed to compare two groups treated with different G-CSF administration schedules with a third group receiving no G-CSF, after autologous peripheral blood stem cell transplantation (APBSCT). Children and adults with haematological malignancies or solid tumours were randomly assigned to receive either 150 mu g/m(2)/day of Lenograstim starting on day 1 (%G1%) or on day 5 (G5) post APBSCT, or no Lenograstim (G0). Randomisation was stratified according to the conditioning regimen (Busulfan vs TBI vs no Busulfan and no TBI) and the graft CD 34+ cell count. A total of 240 patients were randomised; 239 were evaluable. All three patient groups were comparable. Median duration of neutropenia was 9 days (4-40),and 10 days (5-15) in the %G1% and G5 groups, respectively, significantly shorter than in the G0 group, 13 days (7-36) (P < 0.0001). No difference was observed in the duration of thrombocytopenia, transfusion support and extra-haematological complications. The duration of post transplant hospitalisation was significantly shorter in adults who received G-CSF. Clinical and cost arguments favour the initiation of G-CSF on day 5 in adults. The same policy could be applied in children given that clinical management is easier and costs are similar.

2/7/12 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

13333292 Genuine Article#: 870TB Number of References: 8
Title: Effect of filgrastim on serum lactate dehydrogenase and alkaline phosphatase values in early breast cancer patients
Author(s): Papaldo P; Di Cosimo S; Ferretti G (REPRINT) ; Vici P; Marolla P ; Carlini P; Fabi A; Cognetti F
Corporate Source: Regina Elena Inst Canc Res,Div Med Oncol A,Via Elio Chianesi 53/I-00144 Rome//Italy/ (REPRINT); Regina Elena Inst Canc Res,Div Med Oncol A,I-00144 Rome//Italy/(gia.fer@flashnet.it)
Journal: CANCER INVESTIGATION, 2004, V22, N4, P650-653
ISSN: 0735-7907 Publication date: 20040000
Publisher: MARCEL DEKKER INC, 270 MADISON AVE, NEW YORK, NY 10016 USA
Language: English Document Type: LETTER
Abstract: To improve chemotherapy dose intensity and to optimize the use of granulocyte-colony stimulating factor, 506 patients with early breast cancer were randomly assigned to high dose epirubicin and cyclophospamide (EC) with or without prophylactic subcutaneously filgrastim, according to 5 different schedules: 480 mug or 300 mug daily or every other day, on day 8 through day 14, and 300 mug daily on days 8 and 12 of each chemotherapy course, Serum levels of lactate dehydrogenase (LDH) and alkaline phosphatase (AP) were significantly higher in patients given EC plus filgrastim than EC alone (P = 0.0001), the rate of %G1%-3 toxicity being 33.4% and 13.1% vs. 1.6% and 1%, respectively. No clinical evidence of filgrastim-related hepatic damage or significant difference in transaminase and gamma-GT elevation was seen between the two groups. LDH and AP closely resembled peripheral blood leukocytes count and increased with increasing leucocytosis, throughout the 5 schedules. Although no patient continued treatment for filgrastim-related side effects, and LDH and AP rises resolved spontaneously within 3 weeks following the chemotherapy course, physicians should be aware of the transient and innocuous change in serum chemistry associated to leucocytosis, since it could be misinterpreted as expression of disease activity.

2/7/13 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

12425222 Genuine Article#: 765VK Number of References: 43
Title: C/EBP alpha p30, a myeloid leukemia oncoprotein, limits G-CSF receptor expression but not terminal granulopoiesis via site-selective inhibition of C/EBP DNA binding

Author(s): Cleaves R; Wang QF; Friedman AD (REPRINT)
Corporate Source: Johns Hopkins Univ,Div Pediat Oncol, Sidney Kimmel Comprehens Canc Ctr,Canc Res Bldg,Rm 253,1650 Orleans St/Baltimore//MD/21231 (REPRINT); Johns Hopkins Univ,Div Pediat Oncol, Sidney Kimmel Comprehens Canc Ctr,Baltimore//MD/21231
Journal: ONCOGENE, 2004, V23, N3 (JAN 22), P716-725
ISSN: 0950-9232 Publication date: 20040122
Publisher: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
Language: English Document Type: ARTICLE
Abstract: Heterozygous mutations of the CEBPA gene are present in 5% of acute myeloid leukemia (AML) cases and often lead to the expression of an N-terminally truncated, 30 kDa isoform, C/EBPalphap30, from an internal translation start site. We have assessed the effect of C/EBPalphap30 on granulopoiesis utilizing C/EBPalphap30-ER, containing the estradiol receptor ligand-binding domain. In contrast to C/EBPalpha-ER, C/EBPalphap30-ER did not induce 32Dcl3 myeloid cell differentiation in IL-3. However, both isoforms, when expressed at high levels, were capable of inhibiting E2F activity in 32Dcl3 cells and of slowing their %G1% to S progression. C/EBPalphap30 repressed expression of the endogenous G-CSF receptor several-fold. To facilitate investigation of the effect of C/EBPalphap30-ER on granulopoiesis downstream of G-CSF signalling, we coexpressed exogenous G-CSF receptor. C/EBPalphap30-ER/GR cells expressed several granulocytic markers in G-CSF and demonstrated nuclear maturation. Rat C/EBPalpha-ER and C/EBPalphap30-ER, expressed in 293T cells, bound the C/EBP site from the NE gene with similar affinity, as did human C/EBPalpha and C/EBPalphap30. In contrast, C/EBPalphap30 bound the C/EBP sites in the PU.1 or GR gene with 3-6-fold reduced affinity. Thus, the selective inhibition of GR expression by C/EBPalphap30-ER is due in part to its variable affinity for C/EBP sites. Variation in affinity for selected cis elements among isoforms may affect the biology of basic region-leucine zipper (bZIP) proteins.

2/7/14 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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10904759 Genuine Article#: 582WX Number of References: 33
Title: Granulocyte-colony stimulating factor enhances chimeric antibody Nd2 dependent cytotoxicity against pancreatic cancer mediated by polymorphonuclear neutrophils
Author(s): Tamamori Y; Sawada T (REPRINT) ; Nishihara T; Yamashita Y; Ohira M; Ho JJL; Kim YS; Chung KHY
Corporate Source: Osaka City Univ,Grad Sch Med, Dept Surg Oncol, Abeno Ku,1-4-3 Asahi Machi/Osaka 5458585//Japan/ (REPRINT); Osaka City Univ,Grad Sch Med, Dept Surg Oncol, Abeno Ku,Osaka 5458585//Japan/; Univ Calif San Francisco,Vet Adm Med Ctr, Gastrointestinal Res Lab,San Francisco//CA/94121
Journal: INTERNATIONAL JOURNAL OF ONCOLOGY, 2002, V21, N3 (SEP), P649-654
ISSN: 1019-6439 Publication date: 20020900
Publisher: PROFESSOR D A SPANDIDOS, 1, S MERKOURI ST, EDITORIAL OFFICE,, ATHENS 116 35, GREECE
Language: English Document Type: ARTICLE
Abstract: Nd2 is a monoclonal antibody against pancreatic cancer. We have previously reported that human/mouse chimeric antibody Nd2 (c-Nd2) can induce antibody-dependent cell-mediated cytotoxicity (ADCC) with peripheral blood mononuclear cells (PBMs) as effectors. In this study, we investigated whether c-Nd2 can induce ADCC with polymorphonuclear neutrophils (PMNs) as effector cells and the effects of granulocyte-colony stimulating factor (G-CSF) in enhancing this cytotoxicity. Cytotoxicities for pancreatic cancer cell line, SW1990 were dose-dependently increased by c-Nd2 during co-culture with PMNs and these cytotoxicities were significantly suppressed by the addition of neutralizing antibodies against CD16, which is Fcgamma receptor expressed on PMN membranes. PMNs treated with G-CSF significantly enhanced in vitro ADCC activity against SW1990 induced by c-Nd2. The in vivo growth of subcutaneously transplanted SW1990 tumor in nude mouse was significantly inhibited by i.p. administration of c-Nd2 compared to control (non-specific %IgG1%). In addition, this inhibitory effect was enhanced by the combination of c-Nd2 and G-CSF. Immunohistochemical study with anti-mouse neutrophil elastase antibody demonstrated strong infiltrations of PMNs into and around the transplanted tumor, treated with c-Nd2 and G-CSF. These results suggest that PMNs play an important role in c-Nd2 inducing ADCC and that combination immunotherapy of c-Nd2 with G-CSF may have clinical applications in the treatment of patients with pancreatic cancer by enhancing ADCC.

2/7/15 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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10045080 Genuine Article#: 479QA Number of References: 28
Title: The A3 adenosine receptor as a new target for cancer therapy and chemoprotection
Author(s): Fishman P (REPRINT) ; Bar-Yehuda S; Barer F; Madi L; Multani AS; Pathak S
Corporate Source: Tel Aviv Univ,Sackler Fac Med, Rabin Med Ctr, Felsenstein Med Res Ctr,Lab Clin & Tumor Immuno,IL-49100 Petah Tiqwa//Israel/ (REPRINT); Tel Aviv Univ,Sackler Fac Med, Rabin Med Ctr, Felsenstein Med Res Ctr,Lab Clin & Tumor Immuno,IL-49100 Petah Tiqwa//Israel/; Can Fite Biopharma Ltd,Petah Tiqwa//Israel/; Univ Texas,MD Anderson Canc Ctr, Dept Canc Biol,Houston//TX/77030
Journal: EXPERIMENTAL CELL RESEARCH, 2001, V269, N2 (OCT 1), P230-236
ISSN: 0014-4827 Publication date: 20011001
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA
Language: English Document Type: ARTICLE
Abstract: Adenosine, a purine nucleoside, acts as a regulatory molecule, by binding to specific G-protein-coupled A(1), A(2A), A(2B), and A(3) cell surface receptors. We have recently demonstrated that adenosine induces a differential effect on tumor and normal cells. While inhibiting in vitro tumor cell growth, it stimulates bone marrow cell proliferation. This dual activity was mediated through the A3 adenosine receptor. This study showed that a synthetic agonist to the A3 adenosine receptor, 2-chloro-N-6(3-iodobenzyl)-adenosine-5'-N-methyl-uronamide (Cl-IB-MECA), at nanomolar concentrations, inhibited tumor cell growth through a cytostatic pathway, i.e., induced an increase number of cells in the G0/%G1% phase of the cell cycle and decreased the telomeric signal. Interestingly, Cl-IB-MECA stimulates murine bone marrow cell proliferation through the induction of granulocyte-colony-stimulating factor. Oral administration of Cl-IB-MECA to melanoma-bearing mice suppressed the development of melanoma lung metastases (60.8 +/- 6.5% inhibition). In combination with cyclophosphamide, a synergistic antitumor effect was achieved (78.5 +/- 9.1% inhibition). Furthermore, Cl-IB-MECA prevented the cyclophosphamide-induced myelotoxic effects by increasing the number of white blood cells and the percentage of neutrophils, demonstrating its efficacy as a chemoprotective agent. We conclude that A3 adenosine receptor agonist, Cl-IB-MECA, exhibits systemic anticancer and chemoprotective effects. (C) 2001 Academic Press.

2/7/16 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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09442398 Genuine Article#: 405ZA Number of References: 26
Title: Mechanisms of G-CSF- or GM-CSF-stimulated tumor cell killing by Fc receptor-directed bispecific antibodies
Author(s): Stockmeyer B (REPRINT) ; Elsasser D; Dechant M; Repp R; Gramatzki M; Glennie MJ; van de Winkel JGJ; Valerius T
Corporate Source: Univ Erlangen Nurnberg,Div Hematol Oncol, Dept Med 3,Krankenhausstr 12/D-91054 Erlangen//Germany/ (REPRINT); Univ Erlangen Numberg,Div Hematol Oncol, Dept Med 3,D-91054 Erlangen//Germany/; Sch Med,Tenovus Res Lab, Canc Sci Div,Southampton/Hants/England/; Univ Utrecht,Med Ctr, Immunotherapy Lab,Utrecht//Netherlands/; Univ Utrecht,Med Ctr, Genmab Europe,Utrecht//Netherlands/

Journal: JOURNAL OF IMMUNOLOGICAL METHODS, 2001, V248, N1-2 (FEB 1), P 103-111
ISSN: 0022-1759 Publication date: 20010201
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
Language: English Document Type: ARTICLE
Abstract: Studies with gene-modified mice have recently reinforced the importance of Fc receptor-mediated effector mechanisms for the therapeutic efficacy of rituxan and herceptin - two clinically approved antibodies for the treatment of tumor patients. We investigated Fc receptor-dependent tumor cell killing by mononuclear and granulocytic effector cells - comparing human %IgG1% antibodies against CD20 or HER-2/neu with their respective Fc gamma RI (CD64)-, Fc gamma RIII (CD16)-, or Fc alpha RI (CD89)-directed bispecific derivatives. With blood from healthy donors as effector source, human %IgG1% and Fc gamma RIII (CDI6)-directed bispecific antibodies proved most effective in recruiting mononuclear effector cells, whereas tumor cell killing by granulocytes was most potently triggered by Fc alpha RI-directed bispecific constructs. Granulocyte-mediated tumor cell lysis was significantly enhanced when blood from G-CSF- or GM-CSF-treated patients was investigated. Interestingly, however, both myeloid growth factors improved effector cell recruitment by different mechanisms, which were furthermore dependent on the tumor target antigen, and on the selected cytotoxic Fc receptor. (C) 2001 Elsevier Science B.V. All rights reserved.

2/7/17 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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08641539 Genuine Article#: 311FK Number of References: 17
Title: Randomized cross-over trial of progenitor-cell mobilization: High-dose cyclophosphamide plus granulocyte colony-stimulating factor (G-CSF) versus granulocyte-macrophage colony-stimulating factor plus G-CSF
Author(s): Koc ON (REPRINT) ; Gerson SL; Cooper BW; Laughlin M; Meyerson H; Kutteh L; Fox RM; Szekely EM; Tainer N; Lazarus HM
Corporate Source: CASE WESTERN RESERVE UNIV,DEPT MED, BRB-3 HEMATOL ONCOL, 10900 EUCLID AVE/CLEVELAND//OH/44106 (REPRINT); CASE WESTERN RESERVE UNIV,DEPT PATHOL/CLEVELAND//OH/44106; IRELAND CANC CTR,/CLEVELAND//OH/; UNIV HOSP CLEVELAND,/CLEVELAND//OH/44106
Journal: JOURNAL OF CLINICAL ONCOLOGY, 2000, V18, N9 (MAY), P1824-1830
ISSN: 0732-183X Publication date: 20000500
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621
Language: English Document Type: ARTICLE
Abstract: Purpose: patient response to hematopoietic progenitor-cell mobilizing regimens seems to vary considerably, making comparison between regimens difficult. To eliminate this inter-patient variability, we designed a cross-over trial and prospectively compared the number of progenitors mobilized inta blood after granulocyte-macrophage colony-stimulating factor (GM-CSF) days 1 to 12 plus granulocyte colony-stimulating factor (G-CSF) days 7 to 12 (regimen G) with the number of progenitors after cyclophosphamide plus G-CSF days 3 to 14 (regimen C) in the same patient.

Patients and Methods: Twenty-nine patients were randomized ta receive either regimen G or C first(%G1% and C1, respectively) and underwent two leukaphereses. After a washout period, patients were then crossed over to the alternate regimen [C2 and G2, respectively) and underwent two additional leukaphereses. The hematopoietic progenitor-cell content of each collection was determined. In addition, toxicity and charges were tracked.

Results: Regimen C (n = 50) resulted in mobilization of more CD34(+) cells (2.7-fold/kg/apheresis), erythroid burst-forming units(1.8-fold/kg/apheresis), and colony-forming units-granulocyte-macrophage (2.2-fold/kg/apheresis) compared with regimen G given ta the same patients (n = 46;paired t test, P < .01 for all comparisons). Compared with regimen G, regimen C resulted in better mobilization, whether it was given first (P = .025) or second (P = .02). The ability to achieve a target collection of greater than or equal to 2 x 10(6) CD34(+) cells/kg using two leukaphereses was 50% after %G1% and 90% after C1. Three of the seven patients in whom mobilization was poor after %G1% had greater than or equal to 2 x 10(6) CD34(+) cells/kg with two leukaphereses after C2. In contrast, when regimen G was given second (G2), seven out of 10 patients failed to achieve the target CD34(+) cell dose despite adequate collections after C1. Thirty percent of the patients (nine of 29) given regimen C were admitted to the hospital because of neutropenic fever for a median duration of 4 days (range, 2 to 10 days). The higher cost of regimen C was balanced by higher CD34(+) cell yield, resulting in equivalent charges based on cost per CD34(+) cell collected.

Conclusion: We report the first clinical trial that used a cross-over design showing that high-dose cyclophosphamide plus G-CSF results in mobilization of more progenitors then GM-CSF plus G-CSF when tested in the same patient regardless of sequence of administration, although the regimen is associated with greater morbidity. patients who fail to achieve adequate mobilization after regimen G can be treated with regimen C as an effective salvage regimen, whereas patients who fail regimen C are unlikely ta benefit from subsequent treatment with regimen G. The cross-over design allowed detection of significant differences between regimens in a small cohort of patients and should be considered in design of future comparisons of mobilization regimens. (C) 2000 by American Society of Clinical Oncology.

2/7/18 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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07731457 Genuine Article#: 202KA Number of References: 16
Title: Preclinical studies combining bispecific antibodies with cytokine-stimulated effector cells for immunotherapy of renal cell carcinoma
Author(s): Elsasser D (REPRINT) ; Stadick H; Stark S; VandeWinkel JGJ; Gramatzki M; Schrott KM; Valerius T; Schafhauser W
Corporate Source: UNIV ERLANGEN NURNBERG,DEPT UROL, MAXIMILIANSPL 1/D-91054 ERLANGEN//GERMANY/ (REPRINT); UNIV ERLANGEN NURNBERG,DEPT MED 3/D-91054 ERLANGEN//GERMANY/; UNIV UTRECHT HOSP,DEPT IMMUNOL/NL-3508 GA UTRECHT//NETHERLANDS/; UNIV UTRECHT HOSP,MEDAREX EUROPE/NL-3508 GA UTRECHT//NETHERLANDS/
Journal: ANTICANCER RESEARCH, 1999, V19, N2C (MAR-APR), P1525-1528
ISSN: 0250-7005 Publication date: 19990300
Publisher: INT INST ANTICANCER RESEARCH, EDITORIAL OFFICE 1ST KM KAPANDNTIOU-KALAMOU RD KAPANDRITI, POB 22, ATHENS 19014, GREECE
Language: English Document Type: ARTICLE
Abstract: Background: Bispecific antibodies - consisting of a F(ab')-fragment derived from a monoclonal antibody against a tumor epitope as well as of another antibody against a cytotoxic trigger molecule on immune effector cells-can improve the effectiveness of antibody- based tumor therapy. Materials and Methods: We used bispecific antibodies with one specifity against the EGF-receptor; which is overexpressed on the majority of renal cell carcinomas, and another specifity against Fe receptors on human leukocytes (FcyRI/CD64; FcyRIII/CD16 and FcaRI/CD89). As source of effector cells, whole blood fi om patients treated with G-CSF, GM-CSF or IL2/IFN-a was used Cu-51- release assays using various renal cancer cell fines as in tumor targets. Further experiments with Percoll- isolated granulocytes or mononuclear cells from the same donors were performed in order to identify the active effector cell populations. Results: Compared with conventional monoclonal EGF-R directed antibodies (murine lgG2a, humanized %lgG1%), bispecific antibodies induced significantly enhanced cytotoxicity. Highest amounts of tumor cell killing were observed using whole blood from patients treated with G-CSF or GM-CSF in combination with an [FcaRI x EGF-R] bispecific antibody. Under these conditions guanulocytes constituted the most active effector. cell population. Conclusion: The combination of myeloid growth factors and bispecific antibodies offer a promising new approach for the treatment of advanced

renal cell carcinoma.

2/7/19 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

07143241 Genuine Article#: 127WX Number of References: 44
Title: Spontaneous and fas-induced apoptotic cell death in aged neutrophils
Author(s): Tortorella C (REPRINT) ; Piazzolla G; Spaccavento F; Pece S; Jirillo E; Antonaci S
Corporate Source: POLICLIN,MED CLIN 2, DEPT INTERNAL MED IMMUNOL & INFECT/I-70124 BARI//ITALY/ (REPRINT); UNIV BARI,SCH MED, DEPT INTERNAL MED IMMUNOL & INFECT DIS, POLICLIN/I-70124 BARI//ITALY/
Journal: JOURNAL OF CLINICAL IMMUNOLOGY, 1998, V18, N5 (SEP), P321-329
ISSN: 0271-9142 Publication date: 19980900
Publisher: PLENUM PUBL CORP, 233 SPRING ST, NEW YORK, NY 10013
Language: English Document Type: ARTICLE
Abstract: On the basis of the strict analogies between polymorphonuclear cell (PMN) alterations in the aging and depressed functional capacities displayed by apoptotic PMN, we investigated the possible occurrence of age-associated changes in neutrophil apoptosis, either spontaneous or induced by Fas antigen (CD95) activation. In both cases, old subjects exhibited a time course kinetics of neutrophil apoptosis, as assessed by morphologic and quantitative DNA fragmentation analysis, which overlapped that observed in the young. These findings were confirmed by DNA ladder analysis, showing a progressive increase in DNA cleavage products in cells cultured in medium alone or added with agonistic anti-Fas IgM (CH-11) monoclonal antibodies (mAbs), after 12 and 6 hr of incubation, respectively. Aged purified neutrophils constitutively expressed CD95, at levels similar to those observed in the young. Moreover, although we failed to detect Fas ligand expression on PMN surface, treatment of cell cultures with antagonistic anti-Fas %IgG1% (ZB4) mAbs determined a significant inhibition of spontaneous apoptosis in neutrophils from both groups of subjects, thus suggesting that the Fas/Fas ligand system is in fact involved in such an event. The results indicate that the overall intrinsic mechanisms regulating neutrophil cell death are not affected by age. Yet aged neutrophils showed a diminished capacity to be rescued by proinflammatory mediators, such as granulocyte-monocyte colony-stimulating factor, granulocyte colony-stimulating factor, and bacterial lipopolysaccharide, following Fas activation. This may hamper the accumulation of functionally active cells in inflammatory areas in vivo, thus contributing to the increased susceptibility of elderly individuals to life-threatening infections.

2/7/20 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

05929688 Genuine Article#: XH428 Number of References: 40
Title: Characterization of cell cycle status and E2F complexes in mobilized CD34(+) cells before and after cytokine stimulation
Author(s): Williams CD; Linch DC; Watts MJ; Thomas NSB (REPRINT)
Corporate Source: UNIV COLL LONDON,SCH MED, DEPT HAEMATOL, 98 CHENIES MEWS/LONDON WC1E 6HX//ENGLAND/ (REPRINT); UNIV COLL LONDON,SCH MED, DEPT HAEMATOL/LONDON WC1E 6HX//ENGLAND/
Journal: BLOOD, 1997, V90, N1 (JUL 1), P194-203
ISSN: 0006-4971 Publication date: 19970701
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399
Language: English Document Type: ARTICLE
Abstract: Mobilized peripheral blood progenitors (CD34(+) cells) have been shown to be either in the G0 or %G1% phase of the cell cycle. In this study, it is shown that they are small cells with low protein content suggestive of G0. Support for this is provided by showing that the principal E2F complex consists of hypophosphorylated p130, E2F-4, and DP-1. The E2F-4 is more highly phosphorylated than in quiescent T cells. In response to cytokines in vitro, the CD34(+) cells start to enter %G1% within 8 hours and enter S-phase at about 48 hours, As cells enter %G1%, E2F-4 is dephosphorylated to several hypophosphorylated forms and three new DNA-binding com plexes appear, including one containing E2F-4, DP-1, and p107. We suggest that mobilized CD34(+) cells may be maintained in G0 by p130, E2F-4, and DP-1 and the coordinate dephosphorylation of E2F-4 and hyperphosphorylation of p130 may be central to the initiation of proliferation. (C) 1997 by The American Society of Hematology.

2/7/21 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

04638339 Genuine Article#: TY669 Number of References: 33
Title: G-CSF ACCELERATES THE CELL-CYCLING OF HEMATOPOIETIC PROGENITOR CELLS AND ABROGATES THE DECELERATION BY TNF-ALPHA
Author(s): MAHMUD N; KATAYAMA N; ITOH R; OHISHI K; MASUYA M; MINAMI N; SHIKU H
Corporate Source: MIE UNIV,SCH MED,DEPT INTERNAL MED 2,2-174 EDOBASHI/TSU/MIE 514/JAPAN/; MIE UNIV,SCH MED,DEPT INTERNAL MED 2/TSU/MIE 514/JAPAN/; MIE UNIV HOSP,BLOOD TRANSFUS SERV/TSU/MIE 514/JAPAN/
Journal: INTERNATIONAL JOURNAL OF ONCOLOGY, 1996, V8, N3 (MAR), P453-459
ISSN: 1019-6439
Language: ENGLISH Document Type: ARTICLE
Abstract: We examined the effects of granulocyte colony-stimulating factor (G-CSF) on cell-cycling of hematopoietic progenitors in serum-free methylcellulose clonal cultures. Serial observations of the cultures showed hastening of growth of colonies by G-CSF, as determined by evaluating the time for individual colonies of 20 cells to reach 40 cells. G-CSF did not affect the incidence of proliferating cells in each developing colony. Cell-cycle analysis revealed that addition of G-CSF to cultures led to a decrease in the percentage of cells in the %G1% phase of the cell-cycle, thereby indicating that G-CSF can modulate the cell-cycle of hematopoietic progenitors mainly by shortening the period of the %G1% phase. Tumor necrosis factor alpha (TNF alpha) exerted opposite effects on cell-cycling of hematopoietic progenitors to those seen with G-CSF. G-CSF abolished the inhibitory effects of TNF alpha on the cell-cycling of hematopoietic progenitors. These observations indicate positive and negative regulatory roles of C-CSF and TNF alpha, respectively, and their interactions in the regulation of cell-cycling of hematopoietic progenitors.

2/7/22 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

04553990 Genuine Article#: TR339 Number of References: 22
Title: ACCELERATED EPIRUBICIN-IFOSFAMIDE-DACARBAZINE REGIMEN IN PATIENTS WITH ADULT SOFT-TISSUE SARCOMAS
Author(s): MICHELOTTI A; ROMANINI A; GIANNESSI P; BENGALA C; CONTE P
Corporate Source: OSPED SANTA CHIARA,UNITA OPERAT ONCOL MED,V ROMA 67/I-56100 PISA//ITALY/; OSPED SANTA CHIARA,UNITA OPERAT ONCOL MED/I-56100 PISA//ITALY/
Journal: AMERICAN JOURNAL OF CLINICAL ONCOLOGY-CANCER CLINICAL TRIALS, 1996 , V19, N1 (FEB), P78-81
ISSN: 0277-3732
Language: ENGLISH Document Type: ARTICLE
Abstract: Background. Neutropenia and infections are the dose-limiting toxicities of the EID regimen and can cause dose reduction and/or delay in chemotherapy administration. The purpose of this study was to verify if EID + G-CSF is feasible with an acceptable toxicity in a day hospital setting and if G-CSF could allow an increase in the dose intensity of the EID regimen by shortening the intervals between the courses. Patients and Methods: 20 patients with inoperable primary, metastatic or residual disease after surgery or at high risk of recurrence after complete resection, histologically confirmed adult soft tissue sarcoma, entered the study. The dose and schedule of the chemotherapy agents were epidoxorubicin 30 mg/m(2) days 1, 2, 3,

dacarbazine 300 mg/m(2) days 1, 2, 3, and ifosfamide 2500 mg/m(2) with mesna uroprotection days 1, 2, 3. G-CSF, 300 mu g/day subcutaneously, was administered from day 7 for a maximum of 14 days and discontinued when WBC was greater than 10 X 10(9)/L. Courses were repeated "as soon as possible," but never earlier than 10 days from the previous course and at least 48 hours after the last G-CSF injection. Results: A total of 66 EID + G-CSF courses were administered. A G3 and %G4% (WHO) neutropenia occurred in 66% of evaluables courses. Nonhematological toxicity was mild. The median number of G-CSF injections required during any interval between courses was 9 (range: 4-14 injections) and the median interval between courses was 21 days (range: 13-36 days). The median dose intensity at the third course of chemotherapy was 1.15 (range: 0.71-1.62). Conclusion: This study shows that G-CSF allows a moderate increase in the delivered dose intensity of chemotherapy with an acceptable toxicity, Further studies are needed to investigate if this increase in DI may translate into an improved response rate.

2/7/23 (Item 13 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03675309 Genuine Article#: PX033 Number of References: 38
Title: COMBINED ANTITUMOR EFFECTS OF TNF AND G-CSF ON A HUMAN MEDULLOBLASTOMA XENOGRAFT LINE
Author(s): MAEDA H; UOZUMI T; KURISU K; MATSUOKA T; KAWAMOTO K; KIYA K; OGASAWARA H; SUGIYAMA K; MIKAMI T; MONDEN S; HARADA K; MATSUDA Y
Corporate Source: MATSUYAMA RED CROSS HOSP,DEPT NEUROSURG,1 BUNKYO CHO/MATSUYAMA/EHIME 790/JAPAN/; HIROSHIMA UNIV,SCH MED,DEPT NEUROSURG/HIROSHIMA//JAPAN/
Journal: JOURNAL OF NEURO-ONCOLOGY, 1994, V21, N3, P203-213
ISSN: 0167-594X
Language: ENGLISH Document Type: ARTICLE
Abstract: The antitumor effects of TNF and G-CSF on a xenograft line of human medulloblastoma were examined. (Method): 1) A human medulloblastoma xenograft line was transplanted into nude mice. Tumor bearing nude mice were divided into the following eight groups: untreated controls (C); those receiving a subcutaneous injection of G-CSF for one week (%G1%); for four weeks (G2); those receiving an intratumoral injection of TNF for four weeks (Tit); an intravenous injection of TNF (Tiv); those receiving a combination of %G1% and Tit (%G1% + Tit); a combination of G2 and Tit (G2 + Tit); and a combination of G2 and Tv (G2 + Tiv). The relative tumor weight in each group was calculated and any antitumor effects were examined by calculating a tumor growth inhibition ratio. 2) Tumor bearing nude mice were divided into the following two groups: those receiving a subcutaneous injection of G-CSF and an intravenous injection of TNF (G + T); and only an intravenous injection of TNF (T). We evaluated the pathological findings from the tumors at 0 h, 0.5 h, 1 h, 3 h, 6 h, 12 h, 24 h and 48 h after the TNF injection. Routine H.E. staining and immunostaining using antigranulocyte and antimacrophage antibodies were performed. (Results): 1) The tumor growth inhibition ratio was 0.112, 0.190, 0.287, 0.451, 0.347, 0.635, and 0.622 at %G1%, G2, Tit, Tiv, %G1% + Tit, G2 + Tit, G2 + Tiv group. A combined antitumor effect was clearly seen in the G2 + Tit and the G2 + Tv groups. 2) The tumor was fragmented by the infiltration of many inflammatory cells 24 hours after TNF injection. Many more macrophages were observed in the tumors of G + T mice than in the T mice. Granulocytes were observed only in the tumors of the G + T mice.

2/7/24 (Item 14 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02804555 Genuine Article#: ME480 Number of References: 42
Title: CORTICOSTEROIDS DIFFERENTIALLY REGULATE SECRETION OF IL-6, IL-8, AND G-CSF BY A HUMAN BRONCHIAL EPITHELIAL-CELL LINE
Author(s): LEVINE SJ; LARIVEE P; LOGUN C; ANGUS CW; SHELHAMER JH
Corporate Source: NIH,WARREN G MAGNUSON CLIN CTR,DEPT CRIT CARE MED/BETHESDA//MD/20892
Journal: AMERICAN JOURNAL OF PHYSIOLOGY, 1993, V265, N4 (OCT), PL360-L368
ISSN: 0002-9513
Language: ENGLISH Document Type: ARTICLE
Abstract: Human airway epithelial cells play an active role in modulating airway inflammation by elaborating a variety of proinflammatory molecules, including cytokines. The purpose of this study was to define the role of corticosteroids in the regulation of cytokine gene transcription and secretion by human bronchial epithelial cells. In particular, we assessed whether dexamethasone was capable of inhibiting the tumor necrosis factor-alpha (TNF-alpha)-mediated secretion of interleukin-6 (IL-6), interleukin-8 (IL-8), and granulocyte colony-stimulating factor (%G1%-CSF) by a human bronchial epithelial cell line (BEAS-2B). Stimulation with 20 ng/ml of TNF-alpha resulted in significant increases in secretion of immunoreactive IL-6, IL-8, and G-CSF that were maximal at 24 h. TNF-alpha-mediated IL-6, IL-8, and G-CSF secretion was concentration dependent and specific. In addition, stimulation with TNF-alpha resulted in significant increases in the quantity of IL-6, IL-8, and G-CSF mRNA as detected by reverse-transcription polymerase chain reaction. Dexamethasone preconditioning significantly inhibited both the secretion of immunoreactive IL-6 and the accumulation of IL-6 mRNA. Although dexamethasone appeared to reduce both the secretion of immunoreactive IL-8 and accumulation of IL-8 mRNA, the inhibitory effects did not reach statistical significance. Finally, dexamethasone did not inhibit either the secretion of immunoreactive G-CSF or the accumulation of G-CSF mRNA. In summary, our results suggest that corticosteroids have a differential effect on the regulation of cytokine secretion by human bronchial epithelial cells. Although corticosteroids may ameliorate airway inflammation by inhibition of IL-6 secretion, dexamethasone did not prevent the TNF-alpha-mediated increases in IL-8 and G-CSF secretion. This represents a potential mechanism by which corticosteroids may fail to downregulate the chemotaxis, activation, and survival of neutrophils in inflammatory airway disorders. These cytokine pathways and their regulatory mechanisms may have important roles in the pathogenesis and therapy of inflammatory airway disorders.

2/7/25 (Item 1 from file: 94)
DIALOG(R)File 94:JICST-EPlus

04167454 JICST ACCESSION NUMBER: 99A0550879 FILE SEGMENT: JICST-E
Cell Cycle-Dependent Change of the Adhesive Character of CD34+ Progenitor Cells and their VLA-4 Expression.
YAMAGUCHI MIKI (1); IKEBUCHI KENJI (1); HIRAYAMA FUMIYA (1); SATO NORIHIRO (1); SEKIGUCHI SADAYOSHI (1)
(1) Hokkaido Red Cross Blood Center
Rinsho Byori(Japanese Journal of Clinical Pathology), 1999, VOL.47,NO.5, PAGE.439-446, FIG.4, TBL.3, REF.30
JOURNAL NUMBER: Z0687AAS ISSN NO: 0047-1860 CODEN: RBYOA
UNIVERSAL DECIMAL CLASSIFICATION: 591.111.05+591.41
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Review article
MEDIA TYPE: Printed Publication
ABSTRACT: We identified the cell cycle status of CD34+ cells of steady-state bone marrow(BM) and peripheral blood(PB) obtained from healthy volunteers, and those of BM and apheresis PB samples collected from donors who had been administered granulocyte colony-stimulating factor(G-CSF). Regardless of whether G-CSF treatment was undergone, more than 10% of CD34+ cells in the BM was in the S+G2/M phase. In contrast, less than 2% of CD34+ cells in the PB was cycling. After co-culturing BM CD34+ cells with a monolayer of the stromal cell line MS-5 for 1 hour, some cells adhered to the stroma. The percentage of cells in the S+G2/M phase among these adherent cells was higher than that among the non-adherent cells. Flow cytometric analysis revealed that CD34+ cells in mobilized PB expressed less VLA-4 than those in BM and that in in vitro-cultured non-adherent cells exhibited a lower level of VLA-4 expression than adherent cells. In addition, CD34+ cells

in the G0/%G1% phase expressed lower levels of VLA-4 than those in the S+G2/M phase. These findings suggested that the reduced expression of adhesion molecules such as VLA-4 by the progenitor cells in the G0/%G1% phase of the cell cycle result in the release of progenitor cells from the hematopoietic microenvironment to peripheral blood. (author abst.)

2/7/26 (Item 2 from file: 94)
DIALOG(R)File 94:JICST-EPlus

03519603 JICST ACCESSION NUMBER: 98A0389467 FILE SEGMENT: JICST-E
CD34+ progenitor cell transplantation from two HLA-mismatched healthy fathers to two infants with severe aplastic anemia.
YASUI M (1); OKAMURA T (1); CHAYAMA K (1); YOSHIMOTO T (1); INOUE M (1); YAGI K (1); KAWA K (1); PARK Y-D (2); (2) Nara Medical Univ., Nara, JPN
Int J Hematol, 1998, VOL.67,NO.1, PAGE.15-22, FIG.1, TBL.4, REF.25
JOURNAL NUMBER: F0888ABI ISSN NO: 0925-5710 CODEN: IJHEE
UNIVERSAL DECIMAL CLASSIFICATION: 616.15-006.43/.44
LANGUAGE: English COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: Pluripotent stem cells of hematopoiesis are included among CD34+ cells in the blood and bone marrow. After granulocyte-colony stimulating factor (G-CSF) mobilization, 1-2% of the mononuclear cells in the blood are CD34+ cells, which can be obtained by leukapheresis. We performed CD34+ progenitor cell transplantation in two children with severe aplastic anemia (SAA) who lacked HLA-matched donors. The donors were treated with G-CSF, 600 .MU.g/body/day subcutaneously, for 4-5 days. CD34+ cell selection was performed from the apheresis concentrate with mouse anti-CD34 antibody 9C5 and magnet beads coated with sheep anti-mouse %IgG1%. After the transplantation, the patients received tacrolimus to prevent graft-versus-host disease (GVHD). G-CSF was given to both patients. A mean number of 4.96 * 106 CD34+ cells per kilogram of body weight were transplanted. The hematopoietic recovery after the CD34+ cell transplantation was rapid, except for platelets, and acute GVHD was less than or equal to grade I. Case 1, who demonstrated mixed chimerism, anemia and thrombocytopenia after the graft, received a second transplant with intensified preconditioning, and now sustains complete and stable hematopoiesis after a follow-up of 314 days posttransplant. Although Case 2 showed early rejection and received a second transplant, sustained engraftment was never achieved. However, the patient's own hematopoiesis appeared. For SAA patients who do not have HLA-matched donors, this type of approach seems to be a feasible and useful method. However, an intensified preconditioning regimen to overcome the high likelihood of rejection should be employed. (author abst.)

2/7/27 (Item 3 from file: 94)
DIALOG(R)File 94:JICST-EPlus

02990106 JICST ACCESSION NUMBER: 96A0829222 FILE SEGMENT: JICST-E
Influence of G-CSF and M-CSF on the Growth of Rat-originated Osteosarcoma Cells in vitro.
SAKI HIROYOSHI (1); ABE KAZUO (1); ICHIHARA HIDEKI (1); KATO YUKIHIRO (1); TATEMATSU NORICHIKA (1); OKA NOBUMITSU (1)
(1) Gifu Univ., Sch. of Med.
Gifu Daigaku Igakubu Kiyo(Acta Scholae Medicinalis Universitatis in Gifu), 1996, VOL.44,NO.1, PAGE.49-58, FIG.8, REF.43
JOURNAL NUMBER: F0639ABY ISSN NO: 0072-4521 CODEN: GDIKA
UNIVERSAL DECIMAL CLASSIFICATION: 616-006-08-092.4
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: This study was designed to examine the effects of granulocyte colony stimulating factor (G-CSF) and macrophage colony stimulating factor (M-CSF) on an osteosarcoma cell (MSK: the established rat osteosarcoma cell line). Cultured osteosarcoma cells were treated with various doses of G-CSF (%G1%: 200ng/ml, G2: 20ng/ml, G3: 2ng/ml) and M-CSF (M1: 1.6*104IU/ml, M2: 1.6*103IU/ml,M3: 1.6*102IU/ml), then the effects were evaluated using both proliferative and phenotypic activity of the cells. In order to evaluate the proliferation of the cells, DNA content and the number of cells were measured. In order to evaluate the phenotypic activity of the cells, alkaline phosphatase(ALP) activity was measured. Results showed the number of cells, DNA content, and ALP activity were significantly increased ($p<0.05$) in %G1%, G2, M1, M2 (than those in control). Moreover the ALP activity per cell was significantly increased ($p<0.05$) in M2 (than control). In those parameter, there was no significant difference between G3, M3 and control. These results suggested that G-CSF and M-CSF may have some effects on the growth of the osteosarcoma cells in high doses (%G1%, G2, M1, M2). The G-CSF and M-CSF in low dose (G3, M3) showed no effect to the osteosarcoma cell. This also suggested low dose (G3, M3) of G-CSF and M-CSF may have no side effect against the growth of osteosarcoma. (author abst.)

2/7/28 (Item 4 from file: 94)
DIALOG(R)File 94:JICST-EPlus

01630312 JICST ACCESSION NUMBER: 92A0619912 FILE SEGMENT: JICST-E
SPECIAL TOPICS. Effects of BRMs on Nerval Endocrine and Immune Reactions with Special Reference to the Effects on the Improvement of QOL of Cancer Patients. Antitumor effects of TNF and G-CSF on a xenograft line of human medulloblastoma.
KURISU KAORU (1); MAEDA HITOSHI (1); MATSUOKA TAKASHI (1); KIYA KATSUZO (1); OGASAWARA HIDENORI (1); SUGIYAMA KAZUHIKO (1); MIKAMI TAKASHI (1); MONDEN SHUJI (1); UOZUMI TOORU (1)
(1) Hiroshima Univ., School of Medicine
Biotherapy(Tokyo), 1992, VOL.6,NO.8, PAGE.1241-1245, FIG.2, TBL.1, REF.5
JOURNAL NUMBER: L0028AAT ISSN NO: 0914-2223
UNIVERSAL DECIMAL CLASSIFICATION: 577.175.1 616-006-08-092.4
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: Antitumor effects of TNF and G-CSF on a xenograft line of human medulloblastoma were discussed. Method: A human medulloblastoma xenograft line (Med-Fu), which had been established in our laboratory, was transplanted subcutaneously into nude mice. Tumor bearing nude mice were then divided into the following eight groups: non-treated control (C) group, subcutaneous injection of 25.MU.g of G-CSF per head, four times a week for one week(%G1%); the same dosage for four weeks(G2); intratumoral injection of 10,000 JRU of TNF per mouse twice a week for four weeks(Tit), intravenous injection of the same dosage of TNF(Tiv); combination of %G1% and Tit(%G1%+Tit); combination of G2 and Tit(G2+Tit); and combination G2 and Tiv(G2+Tiv). Relative tumor weight in each group was calculated and antitumor effects were discussed in relation to tumor growth inhibition ratio in C group. Results: Tumor growth inhibition ratio(1-T/C) was 0.112, 0.190, 0.287, 0.451, 0.331, 0.643 and 0.622, in that order. In our experiment, combined antitumor effects were clearly seen in G2+Tit and G2+Tiv by Battle-Columbus laboratory method. Conclusion: There was an obvious combined antitumor effect of TNF and G-CSF on a xenograft line of human medulloblastoma. (author abst.)

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